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ABUSE-PROOFED DOSAGE FORM**CROSS-REFERENCE TO RELATED APPLICATIONS**

This application is a division of U.S. patent application Ser. No. 10/718,112, filed Nov. 20, 2003, now U.S. Pat. No. 8,114,383, which claims priority of German Patent Application No. 103 36 400.5, filed Aug. 6, 2003, the entire contents of both of which applications are incorporated herein by reference.

BACKGROUND OF THE INVENTION**1. Field of the Invention**

The present invention relates to an abuse-proofed, thermoformed dosage form containing, in addition to one or more active ingredients with abuse potential (A) optionally together with physiologically acceptable auxiliary substances (B), at least one synthetic or natural polymer (C) and optionally at least one wax (D), wherein component (C) exhibits a breaking strength of at least 500 N, and to a process for the production of the dosage form according to the invention.

2. Description of Related Art

Many pharmaceutical active ingredients, in addition to having excellent activity in their appropriate application, also have abuse potential, i.e. they can be used by an abuser to bring about effects other than those intended. Opiates, for example, which are highly active in combating severe to very severe pain, are frequently used by abusers to induce a state of narcosis or euphoria.

In order to make abuse possible, the corresponding dosage forms, such as tablets or capsules are comminuted, for example ground in a mortar, by the abuser, the active ingredient is extracted from the resultant powder using a preferably aqueous liquid and the resultant solution, optionally after being filtered through cotton wool or cellulose wadding, is administered parenterally, in particular intravenously. An additional phenomenon of this kind of administration, in comparison with abusive oral administration, is a further accelerated increase in active ingredient levels giving the abuser the desired effect, namely the "kick" or "rush". This kick is also obtained if the powdered dosage form is administered nasally, i.e. is sniffed. Since controlled-release dosage forms containing active ingredients with abuse potential do not give rise to the kick desired by the abuser when taken orally even in abusively high quantities, such dosage forms are also comminuted and extracted in order to be abused.

U.S. Pat. No. 4,070,494 proposed adding a swellable agent to the dosage form in order to prevent abuse. When water is added to extract the active ingredient, this agent swells and ensures that the filtrate separated from the gel contains only a small quantity of active ingredient.

The multilayer tablet disclosed in WO 95/20947 is based on a similar approach to preventing parenteral abuse, said tablet containing the active ingredient with abuse potential and at least one gel former, each in different layers.

WO 03/015531 A2 discloses another approach to preventing parenteral abuse. A dosage form containing an analgesic opioid and a dye as an aversive agent is described therein. The colour released by tampering with the dosage form is intended to discourage the abuser from using the dosage form which has been tampered with.

Another known option for complicating abuse involves adding antagonists to the active ingredients to the dosage form, for example naloxone or naltrexone in the case of opi-

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ates, or compounds which cause a physiological defence response, such as for example Radix ipecacuanha=ipecac root.

However, since in most cases of abuse it is still necessary to pulverise the dosage form comprising an active ingredient suitable for abuse, it was the object of the present invention to complicate or prevent the pulverisation preceding abuse of the dosage form comprising the agents conventionally available for potential abuse and accordingly to provide a dosage form for active ingredients with abuse potential which ensures the desired therapeutic effect when correctly administered, but from which the active ingredients cannot be converted into a form suitable for abuse simply by pulverisation.

SUMMARY OF THE INVENTION

Said object has been achieved by the provision of the abuse-proofed, thermoformed dosage form according to the invention which contains, in addition to one or more active ingredients with abuse potential (A), at least one synthetic or natural polymer (C) and optionally at least one wax (D), wherein component (C) exhibits a breaking strength of at least 500 N.

DETAILED DESCRIPTION OF THE INVENTION

The use of polymers having the stated minimum breaking strength, preferably in quantities such that the dosage form also exhibits such a minimum breaking strength, means that pulverisation of the dosage form is considerably more difficult using conventional means, so considerably complicating or preventing the subsequent abuse.

If comminution is inadequate, parenteral, in particular intravenous, administration cannot be performed safely or extraction of the active ingredient therefrom takes too long for the abuser or there is no "kick" when taken orally, as release is not spontaneous.

According to the invention, comminution is taken to mean pulverisation of the dosage form with conventional means which are available to an abuser, such as for example a mortar and pestle, a hammer, a mallet or other usual means for pulverisation by application of force.

The dosage form according to the invention is thus suitable for preventing parenteral, nasal and/or oral abuse of pharmaceutical active ingredients with abuse potential.

Pharmaceutical active ingredients with abuse potential are known to the person skilled in the art, as are the quantities thereof to be used and processes for the production thereof, and may be present in the dosage form according to the invention as such, in the form of the corresponding derivatives thereof, in particular esters or ethers, or in each case in the form of corresponding physiologically acceptable compounds, in particular in the form of the salts or solvates thereof, as racemates or stereoisomers. The dosage form according to the invention is also suitable for the administration of several active ingredients. It is preferably used to administer a specific active ingredient.

The dosage form according to the invention is in particular suitable for preventing abuse of a pharmaceutical active ingredient selected from the group consisting of opiates, opioids, tranquillisers, preferably benzodiazepines, barbiturates, stimulants and other narcotics.

The dosage form according to the invention is very particularly suitable for preventing abuse of an opiate, opioid, tranquilliser or another narcotic selected from the group consisting of N-{1-[2-(4-ethyl-5-oxo-2-tetrazolin-1-yl)ethyl]-4-methoxymethyl-4-piperidyl}propionanilide (alfentanil), 5,5-